Appl. No.: 10/510,063

Amdt. dated 06/30/2006

Reply to Office action of February 1, 2006

Amendments to the Claims:

What is claimed is:

- 1. (Currently Amended) A method of selectively acylating a compound starting taxane comprising at least a first and second secondary hydroxyl groups, the method comprising the steps of
- (a) providing a solution of the <u>starting taxane compound</u> in a solvent; and
- (b) contacting the solution with a hindered base and an acylating agent thereby to selectively acylate the first or secondary hydroxyl group,

wherein the hindered base is selected from the group consisting of pyridine derivatives substituted at least at the 2-position, N,N-diisopropylisobutylamine, N-ethyldicyclohexylamine, triethylamine, triisopropylamine, tripropylamine, imidazole, 1,5-diazabicylo[4.3.0]non-5-ene, 1,4-diazabicylo[2.2.2]octane, and 1,8-diazabicylo[5.4.0]undec-7-ene.

- 2. (Canceled)
- 3. (Original) The method of claim 1, wherein' the acylating agent is an acid halide.
- 4. (Currently Amended) The method of claim $\frac{1}{2}$, wherein the acid halide is an acid chloride.
- 5. (Currently Amended) The method of claim 4 3, wherein the acid halide is selected from the group consisting of benzoyl halide, tigloyl halide, hexanoyl halide, butyryl halide, 2-methylbutyryl halide, phenylacetyl halide, furoyl halide, and *tert*-butyl haloformate.
- 6. (Currently Amended) The method of claim 1 wherein the hindered base is a pyridine derivative <u>substituted at least at the 2-position or a trialkylamine</u>.
- 7. (Currently Amended) The method of claim 5, wherein the trialkylamine hindered base is N-ethyldicyclohexylamine or N,N-diisopropylethylamine.
- 8. (Currently Amended) The method of claim [[4]] 1, wherein the <u>hindered base pyridine</u> derivative is selected from the group consisting of 2,6-lutidine[[,]] and 2,4,6-collidine.
- 9. (Currently Amended) A method of selectively acylating a hydroxyl group located at a C-2' position of a taxane molecule having an unprotected hydroxyl group located at a C-7 position, the method comprising the steps of:
- (a) providing a solution comprising a taxane molecule in an organic solvent, and
- (b) contacting the solution with a hindered base and an acylating agent hereby to selectively

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acylate the hydroxyl group located at the C-2' position, wherein the hindered base is selected from the group consisting of pyridine derivatives substituted at least at the 2-position, N,N-diisopropylisobutylamine, N-ethyldicyclohexylamine, triethylamine, triisopropylamine, tripropylamine, imidazole, 1,5-diazabicylo[4.3.0]non-5-ene, 1,4-diazabicyclo[2.2.2]octane, and 1,8-diazabicylo[5.4.0]undec-7-ene.

- 10. (Original) The method of claim 9, wherein the acylating agent is an acid halide-
- 11. (Currently Amended) The method of claim 9-10, wherein the acid halide is an acid chloride-
- 12. (Original) The method of claim 11 wherein the acid chloride is-selected from the group consisting of benzoyl chloride, tigloyl chloride, hexanoyl chloride, butyryl chloride, 2-methylbutyryl chloride, phenylacetyl chloride, furoyl chloride, and *tert*-butyl chloroformate.
- 13. (Original) The method of claim 12 wherein the acid chloride is benzoyl chloride.
- 14. (Original) The method of claim 12 wherein the acid chloride is tigloyl chloride.
- 15. (Currently Amended) The method of claim 11 12, wherein the hindered base is a pyridine derivative substituted at least at the 2-position or a trialkylamine.
- 16. (Currently Amended) The method of claim 15 wherein the pyridine derivative <u>substituted</u> at least at the 2-position is selected from the group consisting of 2,6-lutidine, and 2, 4, 6-collidine.
- 17. (Currently Amended) The method of claim 15-12 wherein the trialkylamine hindered base is N-ethyldicyclohexylamine or N,N-diisopropylethylamine.
- 18. (Original) The method of claim 9 wherein the organic solvent is tetrahydrofuran.
- 19. (Original) The method of claim 9 wherein the organic solvent solubilizes the taxane molecule at a concentration of at least about 15% by weight.
- 20. (Original) The method of claim 9 wherein selective acylation occurs in about 6 hours or less.
- 21. (Original) The method of claim 9 wherein selective acylation occurs at a temperature of about 40°C or less.
- 22. (Original) The method of claim 9 wherein selective acylation occurs at about ambient temperature.

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- 23. (Original) The method of claim 9 wherein each of the hindered base and the acid halide are present in an amount greater than or equal to about 4 equivalents of the taxane molecule.
- 24. (Original) The method of claim 9 wherein the taxane molecule has the formula:

wherein

R_l is hydrogen;

R₂ is hydrogen, an acyl group or a hydroxyl protecting group;

R₄ is an acetate group;

R₇ is hydrogen, an alkyl group, an aryl group, an ester group, an ether group, a glycoside group, an oxo- group, or a hydroxyl protecting group;

R₁₀ is hydrogen; and

Rx is an amino group, a salt of an amino group, or an amino group that is protected with an amino protecting group.

- 25. (Original) The method of claim 24 wherein Rx is N=CHRc or NHC(O) R_n , wherein Rc is an alkyl group, an aryl group, an arylalkyl group, an vinyl group, or an ether group; and R_n is an alkyl group, an arylalkyl group, a vinyl group, or an ether group.
- 26. (Original) The method of claim 25 wherein Rc is selected from the group consisting of phenyl, 1-methyl-l-propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl, and 2-furanyl.

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- 27. (Currently Amended) The method of claim 25 wherein RN $\underline{R}_{\underline{n}}$ is selected from the group consisting of phenyl; l-methyl-l-propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl, 2-furanyl, and *tert* butoxy.
- 28. (Currently Amended) A method of selectively acylating a taxane molecule, the method comprising the steps of
- (a) providing a solution of tetrahydrofuran and a taxane molecule having the formula:

wherein

R₁ is hydrogen;

R₂ is a benzoyl group;

 $R4 R_4$ is an acetate group;

R₇ is hydrogen;

R₁₀ is hydrogen or an acetate group; and

Rx is N=CHRc or $\frac{-NHC(O)R_N}{-NHC(O)R_n}$, wherein Rc is an alkyl group, an aryl group, an arylalkyl group, an vinyl group, or an ether group; and R_n is an alkyl group, an arylalkyl group, a vinyl group, or an ether group; and

(b) adding 2,6-lutidine or *N* ethyldicyclohexylamine and an acid chloride to the solution thereby to selectively acylate the hydroxyl group located at the C-2' position.

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- 29. (Original) The method of claim 28 wherein R_{10} is hydrogen.
- 30. (Original) The method of claim 28 wherein R_{10} is an acetate group.
- 31. (Original) The method of claim 29 wherein Rx is N=CHRc, and Rc is selected from the group consisting of phenyl, 1-methyl-1-propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl; 2furanyl, and *tert*-butoxy.
- 32. (Original) The method of claim 29 wherein Rx is -NHC(O) R_n , and R_n is selected from the group consisting of phenyl, 1-methyl-1 propenyl, n-pentyl, propyl, 1-methyl-propyl, benzyl, 2-furanyl, and tert-butoxy.
- 33. (Original) The method of claim 30 wherein Rx is N=CHR, and R. is selected from the group consisting of phenyl, l-methyl-l-propenyl, n-pentyl, propyl, l-methyl-propyl, benzyl, 2furanyl, and *tert*-butoxy.
- 34. (Currently Amended) The method of claim 30 wherein Rx is $\frac{-\text{NHC}(O)}{\text{RN}}$ is selected from the group consisting of phenyl, 1-methyl-l-propenyl, n-pentyl, propyl, l-methyl-propyl, benzyl, 2-furanyl, and tert-butoxy.
- 35. (Original) The method of claim 31 wherein the acid chloride is selected from the group consisting of benzoyl chloride, tigloyl chloride, hexanoyl chloride, butyryl chloride, 2-methylbutyryl chloride, phenylacetyl chloride, furoyl chloride, and tert butyl chloroformate.
- 36. (Original) The method of claim 32 wherein the acid chloride is selected from the group consisting of benzoyl chloride, tigloyl chloride, hexanoyl chloride, butyryl chloride, 2-methylbutyryl chloride, phenylacetyl chloride, furoyl chloride. and *tert*-butyl chloroformate.
- 37. (Original) The method of claim 33 wherein the acid chloride is selected from the group consisting of benzoyl chloride, tigloyl chloride, hexanoyl chloride, butyryl chloride, 2-methylbutyryl chloride, phenylacetyl chloride, furoyl chloride, and *tert* butyl chloroformate.

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- 38. (Original) The method of claim 34 wherein the acid chloride is selected from the group consisting of benzoyl chloride, tigloyl chloride, hexanoyl chloride, butyryl chloride, 2-methylbutyryl chloride, phenylacetyl chloride, furoyl chloride, and *tert* butyl chloroformate.
- 39. (Original) The method of claim 28 wherein R_{10} is an acetate group, Rx is -NHC(O) R_n , wherein R_n is phenyl, and the acid chloride is benzoyl chloride.
- 40. (Original) The method of claim 28 wherein R_{10} is an acetate group, R_{x} is -NHC(O) R_{n} , wherein R_{n} is 1-methyl-1-propenyl, and the acid chloride is benzoyl chloride.
- 41. (Currently Amended) The method of claim 28 wherein R_{n10} R_{10} is an acetate group, Rx is -NHC(O) R_n , wherein R_{n5} wherein R_n is n-pentyl, and the acid chloride is benzoyl chloride.
- 42. (Original) The method of claims 1,9, or 28 further comprising the step of crystallizing the acylated compound with at least one solubilizing solvent and optionally at least one antisolvent.
- 43. (Previously Presented) The method of claim 42, wherein the solvent is a halogenated hydrocarbon.
- 44. (Currently Amended) The method of claim 42, wherein the solubilizing solvent is selected form the group consisting of acetone, methyl tert butyl ether, triflourotoluene trifluorotoluene, or THF.
- 45. (Previously Presented) The method of claim 42, wherein the solubilizing solvent is methylene chloride.
- 46. (Previously Presented) The method of claim 42, wherein the solvent is methylene chloride and the antisolvent is hexane.
- 47. (Previously Presented) The method of claim 42, wherein the antisolvent is a hydrocarbon alkane.
- 48. (New) The method of claim 1, wherein the method results in at least about 95% of an ending taxane acylated at the C-2' position and less than about 0.1 % of the starting taxane remains unreacted after the contacting step.
- 49. (New) The method of claim 48, wherein the method results in at least about 99% of an ending taxane acylated at the C-2' position.

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- 50. (New) The method of claim 9, wherein the method results in at least about 95% of an ending taxane acylated at the C-2' position and less than about 0.1 % of the starting taxane remains unreacted after the contacting step.
- 51. (New) The method of claim 50, wherein the method results in at least about 99% of an ending taxane acylated at the C-2' position.
- 52. (New) The method of claim 28, wherein the method results in at least about 95% of an ending taxane acylated at the C-2' position and less than about 0.1 % of the starting taxane remains unreacted after the contacting step.
- 53. (New) The method of claim 53, wherein the method results in at least about 99% of an ending taxane acylated at the C-2' position.